

<p>(51) International Patent Classification <sup>7</sup> :  <b>C07D 403/12, 401/14, 405/14, 403/14, A61K 31/517</b></p>	<p><b>A1</b></p>	<p>(11) International Publication Number: <b>WO 00/21955</b></p> <p>(43) International Publication Date: <b>20 April 2000 (20.04.00)</b></p>
<p>(21) International Application Number: <b>PCT/GB99/03295</b></p> <p>(22) International Filing Date: <b>5 October 1999 (05.10.99)</b></p> <p>(30) Priority Data:  <b>98402496.8</b>      <b>8 October 1998 (08.10.98)</b>      <b>EP</b></p> <p>(71) Applicants (for all designated States except US): <b>ZENECA LIMITED [GB/GB]; 15 Stanhope Gate, London W1Y 6LN (GB). ZENECA-PHARMA S.A. [FR/FR]; "Le Galien", 1, rue des Chauffours, Boîte postale 127, F-95022 Cergy Cedex (FR).</b></p> <p>(72) Inventors; and  (75) Inventors/Applicants (for US only): <b>HENNEQUIN, Laurent, François, André [FR/FR]; Z.I. La Pompelle, Boîte postale 1050, F-51689 Reims Cedex 2 (FR). PASQUET, Georges [FR/FR]; Z.I. La Pompelle, Boîte postale 1050, F-51689 Reims Cedex 2 (FR).</b></p> <p>(74) Agent: <b>BRYANT, Tracey; AstraZeneca plc, Global Intellectual Property, Patents, Alderley Park, Mereside, Macclesfield, Cheshire SK10 4TG (GB).</b></p>	<p>(81) Designated States: <b>AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</b></p> <p><b>Published</b>  <i>With international search report.</i></p>	
<p>(54) Title: <b>QUINAZOLINE DERIVATIVES</b></p>		
<div style="position: absolute; left: 650px; top: 600px;">(I)</div>		
<p>(57) Abstract</p> <p>The invention relates to the use of compounds of formula (I), wherein: ring C is a 5-6-membered heterocyclic moiety; Z is -O-, -NH-, -S- or -CH<sub>2</sub>-; R<sup>1</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxymethyl, di(C<sub>1-4</sub>alkoxy)methyl, C<sub>1-4</sub>alkanoyl, trifluoromethyl, cyano, amino, C<sub>2-5</sub>alkenyl, C<sub>2-5</sub>alkynyl, carboxy, C<sub>3-7</sub>cycloalkyl, C<sub>3-7</sub>cycloalkyl C<sub>1-3</sub>alkyl, or an optionally substituted group selected from phenyl, benzyl, phenylC<sub>2-4</sub>alkyl and a 5-6-membered heterocyclic group; n is an integer from 0 to 5; m is an integer from 0 to 3; R<sup>2</sup> represents hydrogen, hydroxy, halogeno, cyano, nitro, trifluoromethyl, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkylsulphonyl, -NR<sup>3</sup>R<sup>4</sup> (wherein R<sup>3</sup> and R<sup>4</sup>, which may be the same or different, each represents hydrogen or C<sub>1-3</sub>alkyl), or R<sup>5</sup>X<sup>1</sup>- (wherein X<sup>1</sup> represents a direct bond, -CH<sub>2</sub>-, or a heteroatom linker group and R<sup>5</sup> is an alkyl, alkenyl or alkynyl chain optionally substituted by for example hydroxy, amino, nitro, alkyl, cycloalkyl, alkoxyalkyl, or an optionally substituted group selected from pyridone, phenyl and a heterocyclic ring, which alkyl, alkenyl or alkynyl chain may have a heteroatom linker group, or R<sup>5</sup> is an optionally substituted group selected from pyridone, phenyl and a heterocyclic ring, and salts thereof, in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals, processes for the preparation of such compounds, pharmaceutical compositions containing a compound of formula (I) or a pharmaceutically acceptable salt thereof as active ingredients and compounds of formula (I). The compounds of formula (I) and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis.</p>		